Fig. 17

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> Ib-1 Hy2 IL-1 Hy1 rat IL-1Ra pig IL-1Ra Hu sIL-1Ra Hu icIL-1Ra

131 P V Q L T K E S E P S A R - - - T K F Y F E Q S W
130 P V R L T Q L P E N G G W N A P I T D F Y F Q Q C D
156 P V S L T N T P K E P - - C T V T K F Y F Q E D Q
155 P V G L T N T P K A A - - - V K V T K F Y F Q Q D Q
137 P V S L T N M P D E G - - V M V T K F Y F Q E D E
137 P V S L T N M P D E G - - - V M V T K F Y F Q E D E

Decoration 'id-consensus': Box residues that match the Consensus exactly.

Fig.1B

FIGURE 2A

SEQ ID NO.: 12

0 0 0 0	0.0.0.0	0.0.0.0
60 120 180 240 300	360 420 480 540 600	660 720 780 840 900
60 CTACAGCACA GAATCTGTTT TGGTGGCTGG TGCTGGGCTG	360 ACCCAGCCTC TGATTGCAGG AGAAGGCTCT GCTGTGCAGA TTTTCCTGGG	660 CTTCCCTACA CACGCTTCAC GGCCTGGCTG AGAGTGAGCC
50 GTGAGGGAGG CTATTTGGGG CTCACACCCC GCCTGGAGCC	350 CTCTGGCTTC CAGACACCAC TATGCAGACC GCAGACAACT AAGGTCCCCA	650 GAAGAGGGGC GAAGAGGCCA GCTGCTGCCT CTCACCAAGG
40 TCCTCCAACT TGTGGCTCAG ACATCCCAGG AGGCAGAGCT	340 GCACGTCTGC CAGTGAGGAC CATAATTAAA AGATCCTGTT GGACCGCACC	640 TGTGGAGACA CAAAGGTGGT CAGGCTTGAG GCCAGTACAG
30 GCTGGGCTTA TGGGAATTGT GCAAGCACAC AGTCAGGGAG TGGCAGGCCA	330 CTAAGCCCCA TCCTCCCCAT CAAGATACTA TGCTGGTGGG	630 GCCTGGCATG AGGAACTGTA GCTCCGCCTT AGCCCCAGCA
GGCAGTGGGA CTGGGTTTGA CTCCACCCCA CTCTCAGGGC TCCAGTTTCT CAGAACCAGC ACTTGCTCCC GGATAGCCTC GTGGAAGCCT	310 CAGCCCGTGG CTGAGTGGTT CTTTTCTAAC TGCCCTTCTC AATGTGTTCC CTCCCCATGG ATACACAAGA GACGGCCAGC	GATCCAGGGA GGGAGCCGCT GCTGGAGGAT GTGAACATTG CTTCTTCCAG AGCAGCTCAG GTTCCTGTGT GGCCCGGCAG CTCAGCCCGT ACCAAGTTTT
10 GGCAGTGGGA CTCCACCCCA TCCAGTTTCT ACTTGCTCCC	310 CAGCCCGTGG CTTTTCTAAC AATGTGTTCC ATACACAAGA GAAGATCTGC	610 GATCCAGGGA GCTGGAGGAT CTTCTTCCAG GTTCCTGTGT

FIGURE 2B

960 1020 1080 11140 1200	1260 1320
TAGCCTTGTG CCCCCAAACC AAGCTCATCC TGCTCAGGGT CTATGGTAGG CAGAATAATG 960 TCCCCCGAAA TATGTCCACA TCCTAATCC AAGATCTGTG CATATGTTAC CATACATGTC 1020 CAAAGAGGTT TTGCAAATGT GATTATGTTA AGGATCTTGA AATGAGGAGA CAATCCTGGG 1080 TTATCCTTGT GGGCTCAGTT TAATCACAAG AAGGAGGCAG GAAGGGAGAG TCAGAAGAGAG 1140 AATGGAAGAT ACCATGCTTC TAATTTTGAA GATGGAGTGA GGGGCCTTGA GCCAACATAT 1200	GCTTGTGTTT TTAGAAGGAG GAAAAGCCAA GGGAACGGAT TCTCCTCTAT AGTCTCCGA 1260 AGGAACACAG CTCTTGACAC ATGGATTTCA GCTCAGTGAC ACCCATTTCA GACTTCTGAC 1320 CTCCACAACT ATAAAATAAT AAACTTGTGT TATTGTAAAC CTCTGG 1366
950 CTATGGTAGG CATATGTTAC AATGAGGAGA GAAGGGAGAG	TTAGAAGGAG GAAAAGCCAA GGGAACGGAT TCTCCTCTAT GETCTTGACAC ATGGATTTCA GCTCAGTGAC ACCCATTTCA GTAAAATAAT AAACTTGTGT TATTGTAAAC CTCTGG 1366
940 TGCTCAGGGT AAGATCTGTG AGGATCTTGA AAGGAGGCAG	1240 GGGAACGGAT GCTCAGTGAC TATTGTAAAC
930 AAGCTCATCC TCCTAATCCC GATTATGTTA TAATCACAAG	1230 GAAAAGCCAA ATGGATTTCA AAACTTGTGT
920 CCCCCAAACC TATGTCCACA TTGCAAATGT GGGCTCAGTT ACCATGCTTC	1220 TTAGAAGGAG CTCTTGACAC ATAAAATAAT
910 TAGCCTTGTG TCCCCGAAA CAAAGAGGTT TTATCCTTGT	1210 GCTTGTGTTT AGGAACACAG CTCCACAACT

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FIGURE 3

SEQ ID NO.: 13

	20	100	150	200
50	DQTPLIAGMC	CTLPNRGLDR	GEEATRFTFF	QSSSGSAFRL EAAAWPGWFL CQPAEPQQPV QLTKESEPSA RTKFYFEQSW
40	NCPSLLPISE	VADNCCAEKI	DVNIEELYKG	QLTKESEPSA
30	CLWLHPASFS	RDGQLLVGDP	TEEGPSLQLE	CQPAEPQQPV
20	MNGLGNPCSP WLSGSKPQHV CLWLHPASFS NCPSLLPISE DQTPLIAGMC	SLPMARYYII KYADQKALYT RDGQLLVGDP VADNCCAEKI CTLPNRGLDR	GGSRCLACVE	EAAAWPGWFL
10	MNGLGNPCSP	SLPMARYYII	TKVPIFLGIQ GGSRCLACVE TEEGPSLQLE DVNIEELYKG GEEATRFTFF	QSSSGSAFRL

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Figure 4A
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FIGURE 4A

SEQ ID NO.: 14

	09	120	180	240	300			360	420	480	540	009		099	720	780	840	900
09	CTACAGCACA	GAATCTGTTT	TGGTGGCTGG	TGCTGGGCTG	GGAACCCGTG	C C	000	ACCCAGCCTC	TGATTGCAGG	AGAAGGCTCT	GCTGTGCAGA	TTTTCCTGGG	099	CTTCCCTACA	CACGCTTCAC	GGCCTGGCTG	AGAGTGAGCC	AACTGCGTTT
50	GTGAGGGAGG	CTATTTGGGG	CTCACACCCC	GCCTGGAGCC	AATGGCCTGG	C L		CTCTGGCTTC	CAGACACCAC	TATGCAGACC	GCAGACAACT	AAGGTCCCCA	650	TGTGGAGACA GAAGAGGGGC	GAAGAGGCCA	GCTGCTGCCT	CTCACCAAGG	GGAGACAGGA
40	TCCTCCAACT	TGTGGCTCAG	ACATCCCAGG	AGGCAGAGCT	ATTATAGACG	, ,	0 # 0	GCACGTCTGC	CAGTGAGGAC	CATAATTAAA	AGATCCTGTT	GGACCGCACC	640	TGTGGAGACA	CAAAGGTGGT	CAGGCTTGAG	GCCAGTACAG	GAGCTGGTAG
30	GCTGGGCTTA	TGGGAATTGT	GCAAGCACAC	AGTCAGGGAG	TGGCAGGCCA	c c	000	CTAAGCCCCA	TCCTCCCCAT	CAAGATACTA	TGCTGGTGGG	ACAGAGGCTT	630	GCCTGGCATG	AGGAACTGTA	GCTCCGCCTT		ACCAAGITIT ACTITGAACA
20	CTGGGTTTGA	CTCTCAGGGC	CAGAACCAGC	GGATAGCCTC	TGGTGGATTC	C C	320	CTGAGTGGTT	TGCCCTTCTC	CTCCCCATGG	GACGGCCAGC	GAAGATCTGC ACACTTCCTA	620	GATCCAGGGA GGGAGCCGCT	GCTGGAGGAT GTGAACATTG	CTTCTTCCAG AGCAGCTCAG	GTTCCTGTGT GGCCCGGCAG	ACCAAGTTTT
10	GGCAGTGGGA CTGGGTTTGA	CTCCACCCCA CTCTCAGGGC	TCCAGITICI CAGAACCAGC	ACTTGCTCCC	GTGGAAGCCT	(310	CAGCCCGTGG CTGAGTGGTT	CTTTTCTAAC TGCCCTTCTC	AATGTGTTCC CTCCCCATGG	ATACACAAGA GACGGCCAGC	GAAGATCTGC	610	GATCCAGGGA	GCTGGAGGAT	CTTCTTCCAG	GTTCCTGTGT	CTCAGCCCGT

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'IGURE 41

960 1020 1080 1140 1200	1260 1320
960 CAGAATAATG CATACATGTC CAATCCTGGG TCAGAGAGAG	1260 AGTCTCCGGA GACTTCTGAC
TAGCCTTGTG CCCCCAAACC AAGCTCATCC TGCTCAGGGT CTATGGTAGG CAGAATAATG TCCCCCGAAA TATGTCCACA TCCTAATCCC AAGATCTTGT CATATGTTAC CATACATGTC CAAAGAGGTT TTGCAAATGT GATTATGTTA AGGATCTTGA AATGAGGAGA CAATCCTGGG TTATCCTTGT GGGCTCAGTT TAATCACAAG AAGGAGGCAG GAAGGGAGAG TCAGAGAGAGAGAATGT AATGGAAGATT TAATCTACAAG GATGGAGGCAG GAAGGGAGAG GCCAAACATAT	GCTTGTGTTT TTAGAAGGAG GAAAAGCCAA GGGAACGGAT TCTCCTCTAT AGTCTCCGGA AGGAACACAG CTCTTGACAC ATGGATTTCA GCTCAGTGAC ACCCATTTCA GACTTCTGAC CTCCACAACT ATAAAATAAT AAACTTGTGT TATTGTAAAC
940 TGCTCAGGGT AAGATCTGTG AGGATCTTGA AAGGAGGCAG	1240 GGGAACGGAT GCTCAGTGAC
930 AAGCTCATCC TCCTAATCCC GATTATGTTA TAATCACAAG TAATTTTGAA	1230 GAAAAGCCAA ATGGATTTCA AAACTTGTGT
920 CCCCCAAACC TATGTCCACA TTGCAAATGT GGGCTCAGTT ACCATGCTTC	1220 TTAGAAGGAG CTCTTGACAC ATAAAATAAT
910 TAGCCTTGTG TCCCCGAAA CAAAGAGGTT TTATCCTTGT	1210 GCTTGTGTTT AGGAACACAG CTCCACACACT

Protein Bioinformatics Department, Dana Haley, Ph D 10/12/00

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Inventors: Mize et al.

Figure 6

Sheet 9 of 10 3EQ ID NO: 21 SEQ ID NO: 22 Q ID NO: 22

Sequence Alignment based on 2º Structure

Hy2 and IL-1 RA (antagonist)

	\ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \	-2>3>	<4	5	
IL-1RA: 10	MQAFRIWDV	IL-1RA: 10 MQAFRIWDVNQKTFYLRNNQLVAGYLQGPNVNLEEKIDVVPIEPHALFLGIHGGK 64	NLEEKIDVVPIEPHA	LFLGIHGGK 64	SEQ ID NO 21
	+ + I +QK Y	+QK Y R+ QL+ G N EKI ++P	EKI ++P	+FLGI GG	66 (2)4 (1) (2)12
Hy2 : 1 <i>I</i>	ARYYII K YA	ARYYIIKYADQKALYTRDGQLLVGDPVADNCC-AEKICILPNRGLDRTKVPIFLGIQGGS 59	C-AEKICILPNRGLDRTK	VPIFLGIQGGS 59	SEQ ID NO: 22
	\	7> variable dom8>9->	m8>9->	-10->	
IL-1RA: 65	IL-1RA: 65 MCLSCVKSGDETRLOI	DETRIOLEAVNITDLSENRKOL	LEAVNITDLSENRKQDKRFAFIRSDSGPTTSFESAACPGWFLCTA 124	AACPGWFLCTA 124	SEQ ID NO: 21

RCLACVETEEGPSLQLEDVNIEELYKGGEEATRFTFFQSSSGSAFRLEAAAWPGWFLCGP 119 E+AA PGWFLC SEQ ID NO: 22 SEQ ID NO: 21 RF F +S SG IL-1RA: 125 MEADQPVSLTNMPDEGVMVTKFYFQEDE 152 : 120 AEPQQPVQLTKES-EPSARTKFYFEQSW 146 + LQLE VNI +L + TKFYF++ ш CL+CV++ + QPV LT --11-> 09 Hy2

-- 8-strand-->

Hy2

SEQ ID NO:22 = amino acid 7-153 of SEQ ID NO: 2

Figure 6

Figure 7 Sheet 10 of 10

Sequence Alignment based on 2° Structure

Hy2 and IL-1 beta (agonist)

PVADNCCAEK-ICILPNRGLDRT-KVPIFLGI 57 SLQ ID NO. 24	
-11-	LVG D
IL-1β: 63	Hy2 : 1 IL-1 β : 63

SEQ ID NO: 24 = amino acid 5-153--β-strand-->

of SEQ ID NO: 2

Figure 7